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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,490	03/12/2001	Linda Burkly	CIBT-P01-114	2374

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,490	BURKLY ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,9,10,13-25 and 30-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,9,10,13-25 and 30-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 08/04/05, have been entered in full.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/4/05 has been entered.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments.

Maintained Rejections:

Claims 1, 2, 5, 6, 9, 10, 13-19, 21-25, 30, 32, 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patent No: 6,639,051, Wang-EA, in view of Ericson-J et al., Cell 87(661-673)1996 and U.S. Patent No: 4816567 as set forth previously and recast below in view of Applicant's amendments.

Wang teaches methods comprising administering hedgehog agonists to promote epithelial cell growth, including hair growth, and also methods comprising administering hedgehog

antagonists to inhibit epithelial cell growth, including hair growth, see lines 10-22 of col3, lines 39-55 of col 6, lines 24-28 of col 8, lines17-28 of col 9, lines 5-14 of col 11, and topical administration see lines 65 col 11-bridging col 12.

Wang does not however specifically teach that the hedgehog antagonist be an anti-hedgehog antibody, nor that the anti-hedgehog antibody be 5E1 or a humanized antibody. However, the use of anti-hedgehog antibodies as hedgehog antagonists was widely appreciated at the time of the filing of the Wang parent application. For example, Ericson et al. use anti-hedgehog antibody 5E1 as a hedgehog antagonist to block the generation of floor plate cells and motor neurons, see the second to the last paragraph of col 2 of page 661.

The claims also require that the anti-hedgehog antibodies be chimeric antibodies or humanized Both Wang-EA, and Ericson-J et al. appear to be silent with respect to chimeric antibodies, however the optimization of in vivo use of antibodies by making them chimeric antibodies was well established at the time of filing the Wang parent application. U Patent No: 4816567 teaches that in the art of antibody production, monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies and humanized are more preferred, see col 2, lines 40-65, col 5, lines 22-35, col 6, lined48-68, and cols 15 and 16 D.6 and D.7.

Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made, with reasonable expectation of success use anti-hedgehog antibodies as antagonists when practicing the method of Wang, the motivation to do so is provided by both Wang, who teaches that any hedgehog therapeutic that inhibits the activity of wild type hedgehog should be used as a matter of ordinary optimization of operating parameters (col 7, lines 41-43), and by

Ericson who teach that anti-hedgehog antibodies can inhibit the activity of wild type hedgehog (col 2 of page 661), and to further routinely optimize the operation parameters, use 5E1 anti-hedgehog antibody as taught by Ericson, or to make a chimeric, or CDR grafted antibodies or humanized antibodies according to U.S. Patent No: 4816567 when practicing the invention of Wang as modified by Ericson. The motivation to do so is provided by Patent No: 4816567 who teaches that in the art of antibody production, monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies and humanized are more preferred, see col 2, lines 40-65, col 5, lines 22-35, col 6, lined48-68, and cols 15 and 16 D.6 and D.7.

Applicant argues that Ericson merely provide that anti-hedgehog antibodies antagonize hedgehog signaling in a particular in vitro neuronal explant system and provide no motivation to use them in any non-neuronal system such as hair. This argument has been fully considered but not deemed persuasive. It is Wang and not Ericson that provide the motivation to use hedgehog antagonist to inhibit epithelial/hair cells, see above.

Applicant argues that neither Wang or Ericson teach or suggest in that anti-hedgehog antibodies could have there effect on non-neuronal cells and tissues. This argument has been fully considered but not deemed persuasive. Wang teaches methods comprising administering hedgehog agonists to promote epithelial cell growth, including hair growth, and also methods comprising administering hedgehog antagonists to inhibit epithelial cell growth, including hair growth, see lines 10-22 of col3, lines 39-55 of col 6, lines 24-28 of col 8, lines17-28 of col 9, lines 5-14 of col 11, and topical administration see lines 65 col 11-bridging col 12. Neither

Wang nor Ericson suggest that certain antagonists would work on some hedgehog sensitive cells but not other, nor would one of ordinary skill in the art expect such a difference.

Applicant challenges the relevance of the 4816567 patent. This argument has been fully considered but not deemed persuasive. The 4816567 patent demonstrates that in the art of antibody use monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies are more preferred, see col 2, lines 40-65 and cols 15 D.6 and D.7) as is old and well established in the art.

Applicant argues that a non-obvious species is patentable over a patented genus. This is agreed to by the examiner, however, the examiner maintains that the instantly claimed species is obvious in view of Wang and what was commonly known in the art as evidenced by Ericson and the 4816567 patent.

Applicant argues that the prior art does not teach or suggest which specific antibodies to use to inhibit cells of particular tissues. This argument has been fully considered but not deemed persuasive, as the artisan would readily choose the most efficatous anti-body as a matter of routine optimization of operating parameters.

New Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, 9, 13-24, 30-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims require a 5E1 or an AP.G6 antibody, yet neither the prior art nor the instant specification defines a 5E1 or an AP.G6 antibody, thus the skilled artisan could not no whether he or she is practicing the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods and compositions for topically administering a small molecule hedgehog antagonist, does not reasonably provide enablement for such methods and compositions comprising topically administering an anti-hedgehog or patched antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims require methods of topical administration of antibodies, yet the specification describes only the systemic administration of antibodies. The art does not appear to recognize the topical administration of antibodies. One skilled in the art would consider antibodies to be too large for topical administration. For example, cyclosporine (1203 Da) and tarcrolimus (804

Da) are two immunosuppressive agents, similar in size, yet only tacrolimus is adequate for topical administration because cyclosporine is believed to be too large, see the bottom two paragraphs of col 1 of page 559 of Reynolds-NJ et al., Clin Exp. Derm. 27(555-561)2002. An antibody, or effective fragment thereof, would be many times larger than cyclosporine which consists of 12 amino acids.

The specification has provided no specific guidance as to a formulation that would reasonable be expect to be amenable to use as claimed. To find such, if it can be found would be unduly burdensome.

Conclusion

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.
Please note the new central fax number for official correspondence below:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

October 14, 2005